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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|------------------------|-------------|----------------------|-----------------------|------------------|
| 10/533,311 | 04/07/2006 | Francis P. Kuhajda | 029869.00003-US01 | 5370 |
| 85938 | 7590 | 07/10/2009 | EXAMINER | |
| Fox Rothschild LLP | | | JEAN-LOUIS, SAMIRA JM | |
| Phlla, Biotech Group | | | | |
| 2000 Market Street | | | ART UNIT | PAPER NUMBER |
| Philadelphia, PA 19103 | | | 1617 | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/533,311 | KUHAJDA ET AL. | |
| | Examiner | Art Unit | |
| | SAMIRA JEAN-LOUIS | 1617 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 02 April 2009.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-20 is/are pending in the application.
 4a) Of the above claim(s) 9-11, 13-15 and 18 is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 1-8, 12, 16-17, and 19-20 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

| | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ . |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>04/07/06</u> . | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

Election/Restrictions

Claims 1-20 are currently pending in the application

Applicant's election with traverse to various species and election of C-75 as the fatty acid inhibitor and lung tissue as the elected cancer in the reply filed on 04/02/09 is acknowledged. The traversal is on the ground(s) that the prior art is distinct from the instant invention as it teaches a method of ameliorating tumor burden in pre-existing cancer cell growth while the instant invention is directed to the inhibition of cancer development. This is not found persuasive because in the specification of the instant invention, applicant refers to inhibition of cancer as delaying or retarding cancer development in pre-cancerous cells (see specification pg. 8, lines 6-9). Consequently, the Examiner contends that ameliorating tumor burden does indeed encompass delaying or retarding development of cancer by retarding further growth of tumors when left untreated. Given that patent '837 discloses the use of fatty acid synthase in the treatment of cancer, the Examiner maintains that no special technical feature exists. As a result, a lack of unity of invention exists and restriction for examination Purposes was indeed proper.

Thus, the requirement is still deemed proper and is therefore made FINAL.

Claims 9-11, 13-15, and 18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected species, there being no allowable generic or linking claim. Claims 1-8, 12, 16-17, and 19-20 are examined on the merits herein.

IDS

The information disclosure statement (IDS) submitted on 04/07/06 is acknowledged and has been entered. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-5, 8, 12, 16-17, and 19-20 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Kuhajda et al. (Kuhajda et al. PNAS March 2000, Vol. 97,

Nol. 7, pgs. 3450-3454) in view of Wang et al. (Zhonghua Zhong Liu Za Zhi, May 2002, Vol. 24, No. 3, pgs. 271-273).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Kuhajda et al. teach that normal tissues have low levels of fatty acid synthesis while a number of studies have demonstrated high levels of fatty acid synthase (FAS) expression in a wide variety of human malignancies and their precursor lesions (see pg. 3450, left col., Introduction Section, paragraph 1). In fact, Kuhajda et al. teach that the widespread expression of FAS in human cancer and its association with aggressive disease suggests that FAS provides an advantage for tumor growth (see left col., Introduction Section, paragraph 2). Thus, in an effort to study the systemic anticancer effects of FAS inhibition *in vivo*, Kuhajda et al. tested a synthetic, chemically stable inhibitor of mammalian FAS, C75 (i.e. tetrahydro-3-methylene-2-oxo-5-n-octyl-4-furancarboxylic acid; instant claims 1 and 19-20; see pg. 3450, left col., last line and

right col., lines 1-2). Specifically, Kuhajda et al. demonstrated that C75 binds to and inhibits mammalian FAS and inhibits fatty acid synthesis in human cancer cells (instant claim 17; see pg. 3450, right col., Introduction Section, lines 4-6). Importantly, Kuhajda et al. teach that the development of C75 now enables extensive *in vivo* study of FAS inhibition in human cancer (see pg. 3450, right col., Introduction Section, lines 8-11). Moreover, Kuhajda et al. teach that C75 was tested in breast cancer xenografts (i.e. *in vivo*) showed significant anti-tumor activity with concomitant inhibition of fatty acid synthesis via direct inhibition with human FAS (instant claim 17; see pg. 3453, left col., Discussion Section, last paragraph and right col.).

Kuhajda et al. do not specifically teach a method inhibiting lung cancer. Similarly, Kuhajda et al. do not teach treatment in humans or dosage administration.

The Examiner however contends that it is well within the purview of the skilled artisan in view of the teachings of Kuhajda et al. to administer C75 to human patients since cancer occurs in human beings. Additionally, it is well within the purview of the skill of the artisan at the time of the invention to adjust the concentration and dosage of C75 for human consumption during the course of routine experimentation so as to obtain the most effective dosage.

While the percentage of C75 is not disclosed by Kuhajda, it is generally noted that differences in concentration or dosages do not support the patentability of subject

matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Given that applicant did not point out the criticality of a specific range or dosage of the invention, it is concluded that the normal desire of scientists or artisans to improve upon what is already generally known would provide the motivation to determine where in a disclosed set of ranges is the optimum combination of dosages.

Wang et al. teach expression of FAS in non-small cell lung cancer (i.e. NSCLC, a type of lung cancer; instant claims 8 and 12; see pg. 1, abstract). Particularly, Wang et al. analyzed samples of NSCLC patients and found through immunohistochemical techniques that FAS expression rate was 31.4% with expression highest in non-adenocarcinoma human patients (see abstract). Additionally, Wang et al. teach that the survival rate of FAS expression in early lesions of NSCLC patients correlated with poor prognosis (see abstract).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize C75 in non-small cell lung cancer human patients since Wang et al. teach that FAS expression was detected in such patients and associated with poor prognosis and in view of the teachings of Kuhajda who teach inhibition of FAS with C75. Moreover, one of ordinary skill in the art would have found it obvious to optimize the dosage administered through routine examination in order to determine the most

effective dosages for patients. Thus, given the teachings of Kuhajda and Wang, one of ordinary skill in the art would have been motivated to administer C75 to human lung cancer patients with the reasonable expectation of providing a method that is effective in inhibiting cancer development and a method effective in increasing the survival rate of such patients.

Claims 6-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuhajda et al. (Kuhajda et al. PNAS March 2000, Vol. 97, No. 7, pgs. 3450-3454) in view of Wang et al. (Zhonghua Zhong Liu Az Zhi, May 2002, Vol. 24, No. 3, pgs. 271-273) as applied to claims 1-5, 8, 12, 16-17, and 19-20 above and in further view of Hirsch et al. (British Journal of Cancer, May 2002, Vol. 86, pgs. 1449-1456).

The Kuhajda and Wang references are as discussed above and incorporated by reference herein. However, Kuhajda and Wang do not teach that the pre-cancerous lesions express FAS and/or neu protein.

Hirsch et al. teach that the clinical significance of Her-2/neu protein expression in lung cancer is currently under evaluation but certain neu expressing patients show shorter survival (see abstract). Upon investigation of 238 non-small cell lung carcinomas, Hirsch et al. teach that 39 patients express the neu protein wherein 35% of such patients possess adenocarcinomas, 20% large cell carcinomas and 1% squamous cell carcinomas (see abstract). Importantly, Hirsch et al. teach that the findings are

Art Unit: 1617

consistent with previous reports in the literature of NSCLC patients (see pg. 1453, right col., Discussion Section, last paragraph).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize C75 in non-small cell lung cancer human patients who also express neu protein since Hirsch teaches that NSCLC patients also express the neu protein and can lead to shorter survival. Thus, given the teachings of Kuhajda, Wang, and Hirsch, one of ordinary skill in the art would have been motivated to administer C75 to human lung cancer patients with both neu and FAS expression with the reasonable expectation of providing a method that is effective in inhibiting cancer development and a method effective in increasing the survival rate of such patients.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1617

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1617

07/05/2009

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617